Applicants request entry of this amendment in adherence with 37 C.F.R. §§1.821 to 1.825. This amendment is accompanied by a floppy disk containing the above named sequences, SEQ ID NOS:1-18, in computer readable form, and a paper copy of the sequence information which has been printed from the floppy disk.

The information contained in the computer readable disk was prepared through the use of the software program "PatentIn" and is identical to that of the paper copy. This amendment contains no new matter.

Attached hereto is a marked-up version of the changes made to the Specification and Claims by the current Amendment. The attached pages are captioned **"VERSION WITH MARKINGS TO SHOW CHANGES MADE."** As a convenience to the Examiner, a complete set of the Claims, as amended herein, is also attached to this Amendment as an Appendix entitled **"PENDING CLAIMS WITH ENTRY OF THE AMENDMENT."**

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

Paragraph beginning at line 26 of page 5 has been amended as follows:

Figure 1: Figure 1A shows an amino acid of human wild-type TRAC1 (SEQ ID NO:1); Figure 1B shows a cDNA sequence of human wild-type TRAC1 (SEQ ID NO:2); Figure 1C shows a second, slightly shorter cDNA sequence of human wild type TRAC1 (SEQ ID NO:3); Figure 1D shows a cDNA sequence encoding a truncated version of TRAC1 (SEQ ID NO:4; nucleotides 127-891 of SEQ ID NO:3); Figure 1E shows a genomic sequence of human wild type TRAC1 (SEQ ID NO:5); and Figure 1F shows a cDNA (SEQ ID NO:6) and amino acid sequence (SEQ ID NO:7) for mouse wild type TRAC1.

Paragraph beginning at line 11 of page 6 has been amended as follows:

Figure 7 shows that TRAC1 (FLJ20456) (SEQ ID NO:1) is similar to two sequences (SEQ ID NOS:8 and 9) with ring domains.

Paragraph beginning at line 21 of page 6 has been amended as follows:

Figure 13A shows point mutations in conserved cysteine residues of the TRAC1 ring finger domain (SEQ ID NOS:10-17). Figure 13B shows point mutations in the conserved cysteine residues of the TRAC1 ring finger domain disrupt ligase activity.

Paragraph beginning at line 30 of page 12 has been amended as follows:

The terms "identical" or percent "identity," in the context of two or more nucleic acids or polypeptide sequences, refer to two or more sequences or subsequences that are the same or have a specified percentage of amino acid residues or nucleotides that are the same (i.e., about 60% identity, preferably 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or higher identity over a specified region (e.g., a nucleotide sequence of SEQ ID NO:2), when compared and aligned for maximum correspondence over a comparison window or designated region) as measured using a BLAST or BLAST 2.0 sequence comparison algorithms with default parameters described below, or by manual alignment and visual inspection (*see, e.g.*, NCBI web site http://www.ncbi.nlm.nih.gov/BLAST/ or the like). Such sequences are then said to be "substantially identical." This definition also refers to, or may be applied to, the compliment of a test sequence. The definition also includes sequences that have deletions and/or additions, as well as those that have substitutions. As described below, the preferred algorithms can account for gaps and the like. Preferably, identity exists over a region that is at least about 25 amino acids or nucleotides in length, or more preferably over a region that is 50-100 amino acids or nucleotides in length. ~~itu~~

Paragraph beginning at line 22 of page 39 has been amended as follows:

Common linkers such as peptides, polyethers, and the like can also serve as tags, and include polypeptide sequences, such as poly Gly ~~gly~~ sequences of between about 5 and 200 amino acids (SEQ ID NO:18). Such flexible linkers are known to persons of skill in the art. For example, poly(ethelyne glycol) linkers are available from Shearwater Polymers, Inc. Huntsville, Alabama. These linkers optionally have amide linkages, sulfhydryl linkages, or heterofunctional linkages.

In the Claims:

Claims 24 and 33 have been amended as follows:

24. (Amended) A method for identifying a compound capable of interfering with binding of an TRAC1 polypeptide or fragment thereof, the method comprising the steps of:

(i) combining an TRAC1 polypeptide or fragment thereof with an E2 ubiquitin-conjugating enzyme polypeptide and the compound, wherein the TRAC1 polypeptide or fragment thereof is encoded by a nucleic acid that hybridizes under stringent conditions to a nucleic acid encoding a polypeptide having an amino acid sequence of SEQ ID NO:1 ~~SEQ ID NO:2~~; and

(ii) determining the binding of the TRAC1 polypeptide or fragment thereof to the E2 ubiquitin-conjugating enzyme polypeptide.

33. (Amended) An isolated complex comprising a TRAC1 polypeptide or fragment thereof bound to an E2 ubiquitin-conjugating enzyme polypeptide, wherein the TRAC1 polypeptide or fragment thereof is encoded by a nucleic acid that hybridizes under stringent conditions to a nucleic acid encoding a polypeptide having an amino acid sequence of SEQ ID NO:1 ~~SEQ ID NO:2~~.

PENDING CLAIMS WITH ENTRY OF THE AMENDMENT

1. (As filed) A method for identifying a compound that modulates T lymphocyte activation, the method comprising the steps of:

(i) contacting the compound with a TRAC1 polypeptide or a fragment thereof, the polypeptide or fragment thereof encoded by a nucleic acid that hybridizes under stringent conditions to a nucleic acid encoding a polypeptide having an amino acid sequence of SEQ ID NO:1; and

(ii) determining the functional effect of the compound upon the TRAC1 polypeptide.

2. (As filed) The method of claim 1, wherein the functional effect is measured *in vitro*.

3. (As filed) The method of claim 2, wherein the functional effect is a physical effect.

4. (As filed) The method of claim 2, wherein the functional effect is a chemical effect.

5. (As filed) The method of claim 4, wherein the functional effect is determined by measuring ligase activity.

6. (As filed) The method of claim 1, wherein the polypeptide is expressed in a host cell.

7. (As filed) The method of claim 6, wherein the functional effect is a physical effect.

8. (As filed) The method of claim 6, wherein the functional effect is a chemical or phenotypic effect.

9. (As filed) The method of claim 6, wherein the host cell is primary T lymphocyte.

10. (As filed) The method of claim 6,wherein the host cell is a cultured T cell.

11. (As filed) The method of claim 10, wherein the host cell is a Jurkat cell.

12. (As filed) The method of claim 6, wherein the chemical or phenotypic effect is determined by measuring CD69 expression, intracellular Ca2+ mobilization, Ca2+ influx, ligase activity, or lymphocyte proliferation.

13. (As filed) The method of claim 1, wherein modulation is inhibition of T lymphocyte activation.

14. (As filed) The method of claim 1, wherein the polypeptide is recombinant.

15. (As filed) The method of claim 1, wherein the TRAC1 polypeptide comprises an amino acid sequence of SEQ ID NO:1.

16. (As filed) The method of claim 1, wherein the TRAC1 polypeptide is encoded by a nucleic acid comprising a nucleotide sequence of SEQ ID NO:2.

17. (As filed) The method of claim 1, wherein the compound is an antibody.

18. (As filed) The method of claim 1, wherein the compound is an antisense molecule.

19. (As filed) The method of claim 1, wherein the compound is a small organic molecule.

20. (As filed) The method of claim 1, wherein the compound is a peptide.

21. (As filed) The method of claim 20, wherein the peptide is circular.

22. (As filed) A method for identifying a compound that modulates T lymphocyte activation, the method comprising the steps of:

(i) contacting a T cell comprising a TRAC1 polypeptide or fragment thereof with the compound, the TRAC1 polypeptide or fragment thereof encoded by a nucleic acid that hybridizes under stringent conditions to a nucleic acid encoding a polypeptide having an amino acid sequence of SEQ ID NO:1; and

(ii) determining the chemical or phenotypic effect of the compound upon the cell comprising the TRAC1 polypeptide or fragment thereof, thereby identifying a compound that modulates T lymphocyte activation.

23. (As filed) A method for identifying a compound that modulates T lymphocyte activation, the method comprising the steps of:

(i) contacting the compound with a TRAC1 polypeptide or a fragment thereof, the TRAC1 polypeptide or fragment thereof encoded by a nucleic acid that hybridizes under stringent conditions to a nucleic acid encoding a polypeptide having an amino acid sequence of SEQ ID NO:1;

(ii) determining the physical effect of the compound upon the TRAC1 polypeptide; and

(iii) determining the chemical or phenotypic effect of the compound upon a cell comprising the TRAC1 polypeptide or fragment thereof, thereby identifying a compound that modulates T lymphocyte activation.

24. (Amended) A method for identifying a compound capable of interfering with binding of an TRAC1 polypeptide or fragment thereof, the method comprising the steps of:

(i) combining an TRAC1 polypeptide or fragment thereof with an E2 ubiquitin-conjugating enzyme polypeptide and the compound, wherein the TRAC1 polypeptide or fragment thereof is encoded by a nucleic acid that hybridizes under stringent conditions to a nucleic acid encoding a polypeptide having an amino acid sequence of SEQ ID NO:1; and

(ii) determining the binding of the TRAC1 polypeptide or fragment thereof to the E2 ubiquitin-conjugating enzyme polypeptide.

25. (As filed) The method of claim 24, wherein the TRAC1 polypeptide or fragment thereof has ligase activity.

26. (As filed) The method of claim 24, wherein the E2 ubiquitin-conjugating enzyme polypeptide is selected from the group consisting of Ubc5, Ubc7, and Ubc8.

27. (As filed) The method of claim 24, wherein the TRAC1 polypeptide or fragment thereof and the E2 ubiquitin-conjugating enzyme polypeptide are combined first.

28. (As filed) The method of claim 24, wherein the reaction is performed *in vitro*.

29. (As filed) The method of claim 24, wherein the TRAC1 polypeptide or fragment thereof and the E2 ubiquitin-conjugating enzyme polypeptide are expressed in a cell.

30. (As filed) The method of claim 29, wherein the cell is a yeast cell.

31. (As filed) The method of claim 30, wherein the TRAC1 polypeptide or fragment thereof is fused to a heterologous polypeptide.

32. (As filed) The method of claim 24, wherein the binding of the TRAC1 polypeptide or fragment thereof to the E2 ubiquitin-conjugating enzyme polypeptide is determined by measuring reporter gene expression.

33. (Amended) An isolated complex comprising a TRAC1 polypeptide or fragment thereof bound to an E2 ubiquitin-conjugating enzyme polypeptide, wherein the TRAC1 polypeptide or fragment thereof is encoded by a nucleic acid that hybridizes under stringent conditions to a nucleic acid encoding a polypeptide having an amino acid sequence of SEQ ID NO:1.

34. (As filed) The complex of claim 33, wherein the E2 ubiquitin-conjugating enzyme polypeptide is selected from the group consisting of Ubc5, Ubc7, and Ubc8.

35. (As filed) A method of modulating T lymphocyte activation in a subject, the method comprising the step of administering to the subject a therapeutically effective amount of a compound identified using the method of claim 1.

36. (As filed) The method of claim 35, wherein the subject is a human.

37. (As filed) The method of claim 35, wherein the compound is an antibody.

38. (As filed) The method of claim 35, wherein the compound is an antisense molecule.

39. (As filed) The method of claim 35, wherein the compound is a small organic molecule.

40. (As filed) The method of claim 35, wherein the compound is a peptide.

41. (As filed) The method of claim 40, wherein the peptide is circular.

42. (As filed) The method of claim 35, wherein the compound inhibits T lymphocyte activation.

43. (As filed) A method of modulating T lymphocyte activation in a subject, the method comprising the step of administering to the subject a therapeutically effective amount of a TRAC1 polypeptide, the polypeptide encoded by a nucleic acid that hybridizes under stringent conditions to a nucleic acid encoding a polypeptide having an amino acid sequence of SEQ ID NO:1.

44. (As filed) The method of claim 43, wherein the TRAC1 polypeptide comprises an amino acid sequence of SEQ ID NO:1.

45. (As filed) A method of modulating T lymphocyte activation in a subject, the method comprising the step of administering to the subject a therapeutically effective amount of a nucleic acid encoding a TRAC1 polypeptide, wherein the nucleic acid hybridizes under stringent conditions to a nucleic acid encoding a polypeptide having an amino acid sequence of SEQ ID NO:1.

46. (As filed) The method of claim 45, wherein the TRAC1 nucleic acid comprises a nucleotide sequence of SEQ ID NO:2.